

REMARKS

Upon entry of this amendment, claims 24-28, 30-38, 40-41, and 52-53 will be pending in the application. Claims 1-23 and 39 are withdrawn for being drawn to non-elected invention. Claims 29 and 42-51 are cancelled herein. Applicants reserve the right to pursue the subject matter of these claims in one or more continuing applications. Claims 24-28, 30-31, 33-37, 40, and 52 are amended herein. Support for these amendments can be found throughout the as-filed specification, *e.g.*, at least in Examples II and III. No new matter is added.

35 U.S.C. § 112, First Paragraph

Claims 24-28, 30-38, 40, 41, 47, 48, 50, 52, and 53 are rejected under 35 USC § 112, First Paragraph, for lack of enablement. *See*, Office Action at page 3. Claims 47, 48, and 50 are canceled herein. Thus, this rejection, with respect to these claims, is moot and should be withdrawn. Applicants traverse with respect to the pending claims, as amended herein.

The Examiner has alleged that the specification, while being enabling for a method of expanding and differentiating embryonic stem cells and inducing expression of a few proteins expressed by hepatocytes, is not enabling for methods of expanding and transdifferentiating any given stem or progenitor cell into a stem cell that has any particular endodermal cell phenotype. *See*, Office Action at pages 3-4. Applicants disagree.

Regarding cell types suitable for use with the invention as claimed, Applicant wishes to point out that, contrary to the Examiner's assertion, Examples I, II and III disclose the expansion of hepatic stem cells ("oval" cells) and hematopoietic stem cells (CD133+ cord blood cells) according to the claimed method. Thus, the use of stem cells other than ES cells is clearly enabled by instant specification. Regarding the definition of "stem cell", Applicant submits that hematopoietic cells, characterized by CD133 and/or CD34 expression, are commonly referred to in the art as hematopoietic stem cells.

While traversing the Examiner's rejection, and in order to expedite prosecution in this case, independent claim 24 is amended herein to incorporate the subject-matter of now-canceled claim 50. Specifically, amended claim 24 includes the limitations of: ex-vivo expansion of hematopoietic stem or progenitor cells; combination of early acting cytokines; copper chelator reducing available intracellular copper; hepatic growth factor/sodium butyrate; and administration to a subject in need thereof (having a pancreatic disease).

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Support for the amendment to claim 24 is found throughout the instant specification, for example, in Examples II and III, and in original claims 25, 26, 34-36, and 50. Applicants note that reduction to practice of the method as claimed, by transplanting hematopoietic stem/progenitor cells cultured according to step (b) of claim 24 into STZ diabetic mice, resulted in renewed insulin production and effective reconstitution of euglycemia in the STZ-treated mice.

Applicants submit that the subject matter of claim 24, and claims dependent therefrom, is clear and concise, and clearly enabled by the description and working examples disclosed in the instant specification. Thus, Applicants respectfully request withdrawal of the 35 USC § 112, first paragraph rejection.

35 U.S.C. § 112, Second Paragraph

Claims 24-28, 30-38, 40, 41, 47, 48, 50, 52 and 53 are rejected as being indefinite for failing to particularly point out and distinctly claim the subject matter which the Applicant regards as the invention. *See*, Office Action at page 8. Claims 47, 48, and 50 are canceled herein. Thus, this rejection, with respect to these claims, is moot and should be withdrawn. Applicants traverse with respect to the pending claims, as amended herein.

Claim 24 is amended herein to recite a method of treating pancreatic disease in a subject in need thereof, comprising:

- (a) obtaining a population of cells comprising hematopoietic stem and/or progenitor cells;*
- (b) culturing said stem and/or progenitor cells ex-vivo in the presence of:*
 - (i) conditions allowing for cell proliferation, said conditions comprising a combination of early acting cytokines;*
 - (ii) a copper chelator reducing available intracellular copper; and*
 - (iii) at least one hepatic growth factor and/or sodium butyrate; and*
- (c) administering said expanded hematopoietic stem and/or progenitor cells to said subject.*

Claim 28 is amended herein to recite the method of claim 24, wherein the disease is diabetes and the treating is restoration of euglycemia. Support for such an amendment is found, for example, in Examples II and III of the instant specification. Claim 30 is amended herein to clarify the relation of the selection step within the method of independent claim 24.

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Claims 31 and 33 are amended herein to include “selection of CD133+ cells” or “selection of CD133+ or CD34+ cells”, respectively, further clarifying the active step of the selection.

Claim 52 has is amended herein according to the Examiner's suggestion, *i.e.*, to recite proper Markush format.

Thus, Applicants submit that amended claim 24 clearly and concisely points out the claimed subject-matter (method of treatment), and adequately delineates the “metes and bounds” of the invention, and thus claim 24, and claims dependent therefrom, are sufficiently definite. Applicants respectfully request withdrawal of the 35 USC § 112, second paragraph rejection.

35 U.S.C. § 101

Claims 50, 52, and 53 are rejected under 35 U.S.C. § 101 for failing to properly set forth any steps of the claimed process. *See*, Office Action at page 12. Claim 50 is canceled herein. Thus, this rejection, with respect to this claim, is moot and should be withdrawn. Applicants traverse with respect to the pending claims, as amended herein.

Claims 52 and 53 are amended herein to depend from claim 24, which clearly and concisely defines the steps of the claimed process. Applicants respectfully request reconsideration and withdrawal of the 35 USC § 101 rejection.

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CONCLUSION

Applicants submit that the application is in condition for allowance and such action is respectfully requested. However, if upon receipt and review of this amendment, the Examiner believes that the present application is not in condition for allowance and that changes can be suggested which would place the claims in allowable form, the Examiner is respectfully requested to call Applicants' undersigned counsel at the number provided below.

Respectfully submitted,



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